IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:
Raghupathi KANDARAPU et al.
Application No.: 10/596,915
Filed: June 29, 2006
For: PHARMACEUTICAL COMPOSITION

Art Unit: 1611
Examiner: T. M. Love

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

BRIEF ON APPEAL

Further to the Notice of Appeal that was submitted on January 31, 2011, this brief is now being submitted. The brief is due by March 31, 2011, making this submission timely.

The substantive contents of this document are listed in the table on the following page.

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REAL PARTIES IN INTEREST

The real parties in interest are Dr. Reddy's Laboratories Limited and Dr. Reddy's Laboratories, Inc., co-assignees of the entire rights to the application from the inventors.

RELATED APPEALS AND INTERFERENCES

There are no appeals and interferences that are related to this application.

STATUS OF CLAIMS

This application was originally filed with claims 1-20. During prosecution, claims 2, 3, 9-11, 19, and 20 were canceled and claims 21-24 were added. As a result, claims 1, 4-8, 12-18, and 21-24 are currently pending.

All of claims 1, 4-8, 12-18, and 21-24 stand finally rejected and are the subject of this appeal. These claims are listed in the Claims Appendix that begins on page 16 hereof.

STATUS OF AMENDMENTS

All of the amendments that were presented during prosecution have been entered. There was no amendment submitted following the Final Rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

The claims generally pertain to solid pharmaceutical compositions containing a drug compound and/or excipient exhibiting chemically instability in acidic environments. When dosage forms, such as tablets, are coated with an acid-resistant "enteric" coating that allows the dosage forms to pass through the stomach relatively intact, drug and/or excipient instability issues can arise due to the acidic nature of the coating itself.

Independent claim 1 is directed to a solid dosage form, comprising:

(a) a core comprising an acid-sensitive antidepressant active ingredient (described at page 6, lines 12-17);

(b) a subcoating over the core comprising a substance having an amino group that reacts with acidic functional groups (described at page 7, lines 18-31) ; and

(c) an acidic functional group-containing enteric coating over the subcoating (described at page 5, lines 1-9);

wherein a subcoating inhibits interactions between the active ingredient and enteric coating (described at page 7, lines 18-23).

Independent claim 12 is directed to a solid dosage form comprising:

(a) a core comprising an acid-sensitive antidepressant active ingredient having an amino group (described at page 6, lines 1-17);

(b) a subcoating upon the core comprising an α-amino acid (described at page 7, lines 24-31); and

(c) an acidic functional group-containing component in an enteric coating over the subcoating (described at page 5, lines 1-9);

wherein a subcoating inhibits interactions between active ingredient and an enteric coating (described at page 7, lines 18-23).

Independent claim 18 is directed to a solid dosage form comprising:

(a) a core comprising an acid-sensitive antidepressant active ingredient having an amino group (described at page 6, lines 1-17);

(b) a subcoating upon the core comprising glycine (described at page 7, lines 24-31); and

(c) an enteric coating, comprising an acidic functional group-containing component, over the subcoating (disclosed in original claim 18);
wherein a subcoating inhibits interactions between active ingredient and an enteric coating (described at page 7, lines 18-23).

Each of the remaining claims depends from one of these independent claims, and adds at least one limitation thereto.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The claims were finally rejected in an Office Action dated August 30, 2010 (herein, the "Final Rejection"). The issues to be decided in this appeal can be summarized as follows:

A. Whether claims 1, 4-8, 12-18, and 21-24 are unpatentable under 35 U.S.C. § 112, second paragraph, for indefiniteness.

B. Whether claims 1, 4-8, 12-18, and 21-24 are unpatentable under 35 U.S.C. § 103(a), as being rendered obvious by teachings in European Patent Application Publication 0 094 116 A2 of The Procter & Gamble Company (hereinafter, "Close"), in view of U.S. Patent No. 4,804,669 to Lassen (hereinafter, "Lassen").

ARGUMENT

Appellants submit that the rejections of their claims are scientifically and legally improper. The individual rejections will be discussed separately below.

A. Rejections Under 35 U.S.C. § 112, Second Paragraph

In the Final Rejection, it was asserted that independent claims 1, 12, and 18 are not clear, apparently due to perceived defects in the functional limitation language at the end of each claim. As stated on page 3 of the Final Rejection, "... claims 1, 12, and 18 recite '(b) a subcoating on the core ...' and '(c) an acidic functional group containing enteric coating ...'" These limitations are not referred to using exactly this same language in the final functional limitation, which in each claim reads as follows: "wherein a subcoating inhibits interactions between active ingredient and an enteric coating."

According to the Final Rejection, it is unclear whether an additional subcoating is being referred to, a modifier is missing before "active ingredient," and it is unclear whether an additional enteric coating is being referred to. However, Appellants maintain that the claims can be readily interpreted by one having ordinary skill in the art, and there is no valid indefiniteness issue.

The purposes for requiring definiteness in claims are: (1) to provide clear notice to potential infringers regarding what will constitute infringement; and (2) to provide a clear measure of the invention scope for determining patentability. *Warner-Jenkinson Co., Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17 (1997) and *United Carbon Co. v. Binney Co.*, 317 U.S. 228 (1942). It is apparent that the second function is being served, since the claims were regarded as having sufficiently clarity to permit the formulation of a final rejection for obviousness. Also, those skilled in the art would certainly be able to assess whether a particular product infringes.

The definiteness requirement is satisfied if the claims set out and circumscribe a particular area with a reasonable degree of precision and particularity, when considered in the light of teachings of the prior art and of the particular invention. *In re Moore and Janoski*, 439 F.2d 1232 (CCPA 1971).

In patent claims, the articles "a" and "an" are commonly used to refer to one thing or to multiple things. *See, Baldwin Graphic Systems, Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342 (Fed. Cir. 2008):

> ... [t]his court has repeatedly emphasized that an indefinite article 'a' or 'an' in patent parlance carries the meaning of 'one or more' in open-ended claims containing the transitional phrase 'comprising.' That "a" or "an" can mean "one or more" is best described as a rule, rather than merely as a presumption or even a convention. (Citation omitted)

Those skilled in the art will not wonder whether the recitation of "a subcoating" means only one subcoating, or multiple subcoatings, since the claims clearly require that "a subcoating" contains a substance that will react with acidic groups and protect an active ingredient in a coated core from reacting. This principle is clearly described in the specification. Providing more than one subcoating might or might not be beneficial, but either of these situations is readily understood to be encompassed by the claims, as long as the required function is obtained. Similarly, it could not possibly matter for purposes of determining infringement whether one or more enteric coatings is applied to subcoated cores, since the required function still will be obtained.

Regarding the lack of an article before "active ingredient" in the claims, Appellants submit that this does not render the claims indefinite. Those skilled in the art are aware that pharmaceutical dosage forms sometimes contain more than one drug substance. The claims clearly specify that an ingredient in a subcoating will protect an active ingredient in a core from acid-promoted reactions, and it cannot possibly matter which of the contained active ingredients is protected. Grammatically, it might be better to preface "active ingredient" with "an," and Appellants would consider making this amendment before allowance; however, it is not seen as affecting the definiteness of the claims.

The rejection of claims 1, 12, and 18 for indefiniteness is logically and legally improper, and should now be reversed. This will result in claims 4-8, 13-17, and 21-24 being allowable, since they stand rejected only for their depending from a rejected claim.

B. Rejections Under 35 U.S.C. § 103(a).

All of the pending claims stand rejected under this statute, as being unpatentable over Close, in view of Lassen. However, significant differences between the claims and the applied documents have not been addressed in the Final Rejection.

The Close publication is directed to analgesic drug formulations that dissolve in intestinal fluid. The drug of particular interest is aspirin, and granules are prepared by making a core that contains the drug, applying a first coating containing a dispersing agent onto the core, and applying an acid-resistant enteric coating over the first coating. The function of the dispersing agent is to promote a rapid disruption of the enteric coating when the granules reach the alkaline environment of the intestines.

Close mentions glycine as an optional component of the granules in three locations. First, on page 4, at line 25, it is described as being a buffering adjuvant, for inclusion in the drug core. This presumably would be intended to help protect tissues from adverse irritation effects caused by contact with aspirin. Then, on page 5, at lines 15-24, it is described as a dispersing material for inclusion in an "active coating," i.e., a coating that contains a drug (either aspirin or a different drug). All of the examples are consistent with this active coating disclosure, as they use cores that are 90-95% aspirin, coated with a mixture that is 80-85% aspirin, then coated with an enteric polymer composition. The composition of Example II on page 8 includes glycine as an "active coat" ingredient, while Example III includes histidine in that coating.

Lassen discloses the use of the drug compound paroxetine for treating pain. Administration of the drug can be oral or non-oral, with the oral dosage forms being tablets, capsules, powders, granules, liquids, and others. No particular solid formulations of the drugs are described. While Lassen indicates that tablets may have an enteric coating, there is no discussion of how this might be accomplished. Therefore, this document is relevant only for its teachings that paroxetine was previously known as a drug.

In the Final Rejection, on page 5, it was asserted that: (1) all of the active agents of Close have some sensitivity to acid; and (2) the first coating of Close would inhibit interactions between the enteric coating and active. However, all of the active agents disclosed by Close at page 4, lines 3-7 are themselves acidic compounds and would not

require any protection against contact with gastric acid. Moreover, Close contemplates providing the acidic drug compounds in both the cores and the first coating, in which at least a portion of the total contained drug would be in admixture with an excipient such as glycine, and some portion of the drug undoubtedly would be in contact with the enteric coating. It is quite clear that the purposes to be served by the Close compositions do not include preventing the active agent from interacting with the enteric coating. Therefore, both of the assertions in the Final Rejection are incorrect.

Making a literal combination of teachings from Close and Lassen results in compositions where the drug paroxetine would be in contact with the enteric coating, since Close uses large concentrations of drug in the active coating layer. For an acid-sensitive drug, this will not lead to satisfactory pharmaceutical dosage forms – as has been described by the Appellants in their specification. The proposed combination therefore would be at least partially inoperative, and this negates any possible *prima facie* case for obviousness. *In re Fritch*, 973 F2d. 1260 (Fed. Cir. 1992).

In proposing a combination of teachings, it is necessary to consider the entire teachings of the references. According to M.P.E.P. § 2141.03, "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)."

Further quoting from M.P.E.P. § 2143:

> The rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. *KSR*, 550 U.S. at ___, 82 USPQ2d at 1395; *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). "[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR*, 550 U.S. at ___, 82 USPQ2d at 1396.

> If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.

Applying these principles to the present rejection, it is abundantly clear that one cannot simply substitute the paroxetine of Lassen for the aspirin of the Close formulations, to arrive at the invention of the Appellants' claims. Since Lassen does not contain any teachings that would lead a person having ordinary skill in the art to make the necessary modifications to the teachings of Close that would permit the use of paroxetine in the formulations of Close, the holding of obviousness is not supported and the rejection is rendered legally improper.

Therefore, reversal of the rejection of claims 1, 4-8, 12-18, and 21-24 under 35 U.S.C. § 103(a) is requested.

CONCLUSION

As discussed above, the rejection of claims 1, 4-8, 12-18, and 21-24 under 35 U.S.C. § 112, second paragraph is based on a misapprehension of the meanings of the articles "a" and "an." There is no indefiniteness, and reversal of this rejection is requested.

The rejection of claims 1, 4-8, 12-18, and 21-24 under 35 U.S.C. § 103(a), not being in accordance with established legal principles, has not made out a case for obviousness. Accordingly, reversal of this rejection also is requested.

Respectfully submitted,

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CLAIMS APPENDIX

1. A solid dosage form comprising:

(a) a core comprising an acid-sensitive antidepressant active ingredient;

(b) a subcoating upon the core comprising a substance having an amino group that reacts with acidic functional groups; and

(c) an acidic functional group-containing enteric coating over the subcoating; wherein a subcoating inhibits interactions between active ingredient and an enteric coating.

4. The solid dosage form of claim 1, wherein the substance that reacts with acidic functional groups comprises an α-amino acid.

5. The solid dosage form of claim 1, wherein the substance that reacts with acidic functional groups is selected from glycine, alanine, valine, leucine, isoleucine, serine, threonine, methionine, cysteine, aspartic acid, asparagine, glutamic acid, glutamine, arginine, lysine, histadine, phenylalanine, tyrosine, tryptophan, and proline.

6. The solid dosage form of claim 1, wherein the substance that reacts with acidic functional groups comprises about 0.1 to about 12 percent of the dosage form weight.

7. The solid dosage form of claim 1, wherein the substance that reacts with acidic functional groups comprises about 0.5 to about 9 percent of the dosage form weight.

8. The solid dosage form of claim 1, wherein the substance that reacts with acidic functional groups comprises about 0.7 to about 7 percent of the dosage form weight.

12. A solid dosage form comprising:

(a) a core comprising an acid-sensitive antidepressant active ingredient having an amino group;

(b) a subcoating upon the core comprising an α-amino acid; and

(c) an acidic functional group-containing component in an enteric coating over the subcoating;

wherein a subcoating inhibits interactions between active ingredient and an enteric coating.

13. The solid dosage form of claim 12, wherein the substance that reacts with acidic functional groups is selected from glycine, alanine, valine, leucine, isoleucine, serine, threonine, methionine, cysteine, aspartic acid, asparagine, glutamic acid, glutamine, arginine, lysine, histadine, phenylalanine, tyrosine, tryptophan, and proline.

14. The solid dosage form of claim 12, wherein a reaction product of the α-amino acid with the acidic functional group-containing component is water-soluble.

15. The solid dosage form of claim 12, wherein the amino acid comprises about 0.1 to about 12 percent of the dosage form weight.

16. The solid dosage form of claim 12, wherein the amino acid comprises about 0.5 to about 9 percent of the dosage form weight.

17. The solid dosage form of claim 12, wherein the amino acid comprises about 0.7 to about 7 percent of the dosage form weight.

18. A solid dosage form comprising:

(a) a core comprising an acid-sensitive antidepressant active ingredient having an amino group;

(b) a subcoating upon the core comprising glycine; and

(c) an enteric coating, comprising an acidic functional group-containing component, over the subcoating;

wherein a subcoating inhibits interactions between active ingredient and an enteric coating.

21. The solid dosage form of claim 1, wherein the antidepressant active ingredient has an amino group.

22. The solid dosage form of claim 1, wherein an antidepressant active ingredient is one of amitryptyline, amoxapine, bupropion, desipramine, doxepin, duloxetine, fluoxetine, fluvoxamine, imipramine, maprotiline, mirtazapine, nefazodone, nortriptyline, paroxetine, phenelzine, protriptyline, sertraline, tranylcypromine, trazodone, trimipramine, venlafaxine, or any pharmaceutically acceptable salt thereof.

23. The solid dosage form of claim 12, wherein an antidepressant active ingredient is one of amitryptyline, amoxapine, bupropion, desipramine, doxepin, duloxetine, fluoxetine, fluvoxamine, imipramine, maprotiline, mirtazapine, nefazodone, nortriptyline, paroxetine, phenelzine, protriptyline, sertraline, tranylcypromine, trazodone, trimipramine, venlafaxine, or any pharmaceutically acceptable salt thereof.

24. The solid dosage form of claim 18, wherein an antidepressant active ingredient is one of amitryptyline, amoxapine, bupropion, desipramine, doxepin, duloxetine, fluoxetine, fluvoxamine, imipramine, maprotiline, mirtazapine, nefazodone, nortriptyline, paroxetine, phenelzine, protriptyline, sertraline, tranylcypromine, trazodone, trimipramine, venlafaxine, or any pharmaceutically acceptable salt thereof.

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.